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A CONSIDERATION OF THE PROPERTIES OF POISONOUS FUNGI

William W. Ford and Ernest D. Clark

Introduction

The collection of edible fungi, commonly spoken of as mushrooms in contradistinction to the poisonous varieties known as toadstools, has become more and more popular during the past few years in America. On the one hand, the number of well-trained mycologists who undertake the study of fungi during the summer months as a scientific pastime, regardless of the dietetic value of the material they obtain, has been greatly augmented by those individuals who look everywhere for the edible species which they have learned to identify with great accuracy. In consequence, mushroom collecting has become something of a fad in many of our summer resorts and during September and October the fields and pastures are pretty thoroughly searched for such species as the meadow mushroom, *Agaricus campestris*. On the other hand, this country has seen, during the past decade, a great influx of peasants from Italy, Hungary and Bohemia where even the children know the difference between poisonous and harmless mushrooms. As a result, many of the edible species of fungi which grow in the woods are gathered by this foreign-born population either for themselves or for sale in the local markets. In consequence of this greater interest in the subject, mushroom poisoning has become somewhat more common in America despite the warnings issued from time to time, both to native Americans who are ignorant of the first principles of mycology, and to our foreign-born citizens who are misled by the variations in color and other properties which fungi exhibit in different countries. Poisoning by fungi, however, is by no means a modern occurrence. Indeed, mushrooms have been collected from time immemorial, according to Paulet,[1] in such countries as Russia, China, Hungary, Italy, and especially in Tuscany; being exhibited for sale in the public markets in cities like Pekin, St. Petersburg, and Florence.

It is also well known that the ancient Babylonians and the early Romans employed mushrooms in great quantity both as delicacies for the rich and as daily food for the poorer classes.

In early times, knowledge of the properties of fungi must have been gained entirely from experience and the accurate training of the peoples of the old world in the distinctions between the poisonous and harmless varieties could only have been obtained from many accidents. How common mushroom poisoning actually was, however, is not known to us. It must have been fairly frequent since the deaths of several notables from this cause have been recorded in history, not as occurring from some unexplained phenomenon but from accidents of a nature well-recognized by their contemporaries. Of such victims may be mentioned the family of the Greek poet Euripides, including his wife, two sons, and a daughter; Pope Clement VII; Emperor Jovian; Emperor Charles VI; Emperor Claudius; and a number of others.[2] Coming down to more modern times our first definite knowledge of the number of fatalities from mushrooms came from Paulet[1] who states that from the year 1749 to 1788 there were a hundred deaths in the environs of Paris alone. About the time of Paulet, Bulliard,[3] the celebrated French mycologist, began to systematize the knowledge of fungi possessed by men of his generation, established the various species upon firm ground, gave accurate descriptions of their botanical characters, and pointed out their physiological properties. Indeed, many of the species of the present day were established by this tireless French mycologist.

More recently, our knowledge of the extent to which mushroom fatalities may occur in France has been augmented by the publications of Bardy[4] who reported 60 cases in that district known as Les Vosges, and of Guillaud[5] who estimated the number of deaths in the southwest of France at about 100 annually. Falck[6] has also reported 53 cases in Germany with 40 deaths, and at the same time Inoko[7] in Japan has reported over 480 cases of mushroom intoxication in eight years. In this country Palmer,[8] of Boston, collected 33 cases with 21 deaths and Forster,[9] of Charlestown, 44 cases with 14 fatalities. Finally, in 1900 Gillot[10] found over 200 authentic cases of mushroom poisoning mostly in France and Ford,[2] a few years later, added nearly as many more found in the German, English and French literature since 1900. More recently Clark and Smith[11] have called attention to the great increase of mushroom poisoning in this country and have indicated that many of these cases take place within a few days' time. Thus, in September 1911, 22 deaths occurred in the vicinity of New York City in one period of ten days. The same point is also clear in the recent statistics given for France by Sartory[12] who records 249 cases of fungous poisoning with 153 deaths due chiefly to *Amanita phalloides* and a few *Entoloma lividum.* Of these, 90 per cent. occurred in the short time between August 26th and September 10th, 1912. Finally, one of the best of the modern French publications on poisonous fungi is that of Ferry[13] former editor of the Revue Mycologique who has given an excellent account of the most recent work in this field. A number of different species of mushrooms are poisonous, the symptoms which occur depending upon the presence of definite chemical substances in the plants. This can best be illustrated by a consideration of each species independently.

POISONING BY AMANITA PHALLOIDES BULLIARD

Botanical features

The vast majority of cases of mushroom intoxication are caused by *Amanita phalloides,* the white or deadly Amanita. The earlier species such as *Amanita bulbosa* Persoon and its varieties, *alba, citrina, virescens* and *olivacea, Agaricus bulbosus* Bulliard, *Amanita viridis* Persoon, *Amanita venenosa* Persoon and a number of others are without doubt identical with *Amanita phalloides.* In older French literature it is known as "l'orange ciguë," "l'orange blanche ou citronée," "l'orange ciguë jaunâtre" and "l'orange souris" and in the German as "Knollblätterschwamm." This species has a characteristic appearance and should be readily recognized by collectors of even limited experience. It usually grows to a height of 5–7 inches and its white spores, its ring or annulus and its base or cup (frequently called the poison cup) render its identification comparatively simple. The colors of the pileus, varying from brownish amber to yellow, are important, but are not as a rule regarded as of specific value. In Europe the pileus is usually greenish in color, but in America the greenish color is rarely seen. *Amanita phalloides* usually grows in the woods but this rule is by no means univeral. Occasionally, plants are to be found out in the open pastures near the margin of dense forests or in the grassy spots in the roads leading to and from them.

Clinical aspects

In poisoning by *Amanita phalloides* the clinical symptoms are practically always the same. After a prodromal stage of six to fifteen hours in which no discomfort is felt, the victims are suddenly seized by severe abdominal pain, cramp-like in character, and accompanied by vomiting and diarrhoea. Vomitus and stools consist of undigested food with much blood and mucus. Anuria is usually present and rarely constipation develops. Hemoglobinuria does not occur. Paroxysms of pain and vomiting alternate with periods of remission, the extreme suffering producing the Hippocratic facies described by the French as "la face vulteuse." The loss of strength is rapid and excessive. Jaundice, cyanosis, and coldness of the skin develop within a few days, followed by profound coma from which the patient does not rally. There is no fever. Convulsions are absent in the early stages and when present in the late stages are usually a terminal event. Ocular symptoms also do not usually occur. The course of the disease lasts four to six days in children and eight to ten in adults but if large quantities of the fungus are eaten a very profound intoxication develops and death may occur within 48 hours. The mortality in "phalloides" intoxication is extremely high, varying from 60 to 100 per cent., and is dependent somewhat upon the amount of the poisonous material ingested and probably somewhat upon the treatment. It requires surprisingly small quantities, however, to bring on fatal consequences and there are numerous deaths on record from eating one or two good-sized specimens. Plowright[14] has reported the death of a child of ten years from the consumption of about a third of the top of a small plant eaten raw. Recovery after ingestion of any quantity of *Amanita phalloides* may be regarded as extremely rare but not impossible. There is no difficulty in distinguishing between a poisoning due to this fungus from one due to other species such as *Amanita muscaria* since the entire clinical course of the disease is different.

Autopsies upon individuals killed by *Amanita phalloides* have been carried out by a number of observers but our knowledge of the lesions is by no means satisfactory. There is little to be found to account for the violent paroxysms of pain, vomiting, and diarrhoea. Death seems to be due to the extreme fatty degeneration of the liver. The poisoning resembles most closely phosphorus poisoning (Ford[15]).

Poisonous constituents

The first attempt to obtain the active principle or poison of *Amanita phalloides* is probably that of Letellier,[16] who in 1826 obtained a heat-resistant substance from a number of fungi and to his investigations we owe the term amanitin. Many years subsequently he took up the work again in association with Speneux[17] examining this time a fungus known as *Hypophyllum crux melitense* (Paulet) and probably a variety of *Amanita phalloides.* In this investigation two substances were found, one of an irritating nature, acting upon the mucous membranes of the alimentary canal, and the other heat-resistant substance characterized as a glucosidal alkaloid and identical with the amanitin of Letellier. In 1866 Boudier[18] made an elaborate chemical analysis of *Amanita phalloides* obtaining about a dozen different substances. He ascribed the poisonous action of the plant to an alkaloid but was never able to isolate such a substance although he gave it the name bulbosine. Later, in 1877, Oré[19] also concluded, on biological grounds alone, that *Amanita phalloides* must contain an alkaloid and he gave this hypothetical poison the name phalloidin.

The observations of all these men are interesting now only historically as the names ascribed by these various investigators to the active principle of *Amanita phalloides* are no longer employed except occasionally in French literature. Modern knowledge of the properties of this plant dates from the work of Kobert[20] who established the important fact that extracts of *Amanita phalloides* contain a substance which lakes or dissolves the blood corpuscles of many animals and of man. There were certain serious objections to regarding this substance as the active principle, especially the fact that this blood-laking or hemolytic material is very easily destroyed by moderate heat, much less than is usually employed in cooking, and that individuals dying of *Amanita phalloides* intoxication do not show symptoms which are to be ascribed to this kind of a poison. Nevertheless, Kobert at once jumped to the conclusion that this blood-laking substance which he named phallin was the essential poison of the plant and his discovery was hailed everywhere as one throwing brilliant light upon this most obscure poisoning. The term phallin has gotten into mycological literature all over the world and the idea that *Amanita phalloides* intoxication is due to this remarkable substance which dissolves or eats up the blood corpuscles has something so romantic about it that few have cared to question the correctness of Kobert's conclusions. Kobert himself, however, discovered that blood-laking materials were lacking from many specimens which he afterwards collected and identified as *Amanita phalloides* but that the plants did contain an alcohol-soluble substance which was extremely poisonous to animals. This latter substance he regarded as an alkaloid while phallin he placed in the group of protein-like poisons known as toxalbumins.

Subsequent work upon *Amanita phalloides* has been conducted chiefly by American investigators. It was first shown by Ford[21] that extracts of *Amanita phalloides* contain the hemolytic material described by Kobert and in addition a heat resistant body which will reproduce in animals the majority of the lesions described in fatal cases of *Amanita phalloides* intoxication in man. These two substances were named by him the amanita-hemolysin and the amanita-toxin. The further chemical study upon the plant was carried out by Abel and Ford,[22] by Schlesinger and Ford[23] and Ford and Prouty.[24] According to their investigations *Amanita phalloides* always contains two poisons, the hemolysin and the toxin. The hemolysin is a highly complex glucoside, insoluble in alcohol, easily destroyed by heat and by the action of the digestive juices. While this substance may play a rôle in cases of phalloides intoxication in man there is little or no evidence that it does so under ordinary circumstances. It is present in such a great amount in the plant, however, that the possibility of its having a poisonous action when the fungus is eaten raw or when the digestive secretions are altered in character can not be entirely eliminated. The active principle of the plant is the alcohol-soluble toxin. This resists the action of heat, of drying, and of the digestive juices and reproduces in animals the lesions of phalloides intoxication in man. Chemically, the toxin cannot be characterized definitely but the purest preparations do not give the reactions of either proteins, glucosides, or alkaloids. Fungi cooked by the same methods which are employed in the kitchen are entirely free from hemolysin but have a poisonous action upon animals which is identical with that seen with the amanita-toxin. With our present knowledge the amanita-toxin may be regarded as the active principle or essential poison of *Amanita phalloides.*

Treatment

There is no satisfactory method of treating individuals poisoned by the deadly amanita. It is essential that competent medical advice be obtained as soon as possible and every effort made to rid the alimentary canal of the noxious material in the hope of doing so before enough poison is absorbed to bring on fatal results. Active emetics and purgatives should be administered at once and in case these are not effective the stomach should be washed out and the lower bowel irrigated. Even then, it is frequently impossible to prevent the absorption of the poison which takes place with great rapidity. In the later stages stimulants should be employed with great freedom in the hope of tiding the patient over the periods of weakness. Narcotics should be employed to relieve the intense pain and whenever convulsive movements are seen. *Atropin has no effect in Amanita phalloides intoxication* and no reliance should be placed upon the drug in poisoning by the deadly amanita. Efforts to manufacture a curative serum by the immunization of animals with the poisons in this fungus have thus far been unsuccessful.

POISONING BY OTHER WHITE AMANITAS

A number of other amanitas have poisonous properties identical in all respects with *Amanita phalloides.* The most important of these are *Amanita verna,* the " destroying angel " of Bulliard, which is far more common in America than the true *Amanita phalloides, Amanita virosa* Fries, *Amanita spreta* Peck and *Amanita phalloides* variety *citrina.* All these species are recognized to be deadly poisonous. In addition there are some closely related amanitas which are either of known poisonous character or which have long been regarded as suspicious, the examination of which in the laboratory indicates the possession of definite poisonous action upon animals. This action should undoubtedly be ascribed to the amanita-toxin which is present in all these species in small quantities. This group includes *Amanita porphyria* Albertini & Schweinitz, *Amanita strobiliformis* Vittadini, *Amanita radicata* Peck, *Amanita chlorinosma* Peck, *Amanita mappa* (Batsch) Fries, *Amanita morrisii* Peck, *Amanita citrina* Persoon and *Amanita crenulata* Peck. In this group should also be placed *Amanitopsis volvata* (Peck) Saccardo. All these species should be put in the group of deadly poisonous mushrooms by mycologists and be sedulously avoided by collectors (Ford[25]).

POISONING BY AMANITA MUSCARIA LINNAEUS

Botanical features

Poisoning by *Amanita muscaria* or the "fly agaric" is, next to that following the ingestion of *Amanita phalloides,* the most frequent variety of mushroom intoxication. This is primarily due to the great abundance of this species and its wide distribution over the surface of the world. The *Amanita muscaria,* in addition, more than other fungi is subject to great variations in color, size, and markings due to geographical distribution and seasonal changes. This may possibly account for the numerous accidents in America resulting from mistaking *Amanita muscaria* for *Amanita caesarea,* one of our most beautiful and highly prized edible amanitas. Accidents of this nature have occurred most frequently among foreigners, a fact which seems to indicate the closest resemblance between specimens of certain European species and other American species. The following description of *Amanita muscaria* taken from Farlow[26] brings out the essential botanical features of the plant and a little careful observation of growing fungi should enable collectors to distinguish *Amanita muscaria* from *Amanita caesarea* without hesitation. This is especially true in view of the yellow gills and striking white volva of Caesar's agaric.

"The fly agaric (*Amanita muscaria*), so called because decoctions of it are used in killing flies, is in most places, at least in the northern and eastern parts of the country, a common species—often a good deal more abundant than the common mushroom. It is found during the summer along roadsides, on the borders of fields, and especially in groves of coniferous trees. It prefers a poor soil, of gravelly or sandy character, and occurs only exceptionally in the grassy pastures preferred by the common mushroom. It grows singly and not in groups, and attains a large size, being one of the most striking toadstools. It differs from the common mushroom in having gills which are always white, never pink or purple, and in having a hollow stem which is bulbous at the base and clothed with irregular, fringy scales on all the lower part. The pileus varies in color from a brilliant yellow to orange and a deep red, the yellow and orange being more frequent than the red. The surface is polished [and sometimes sticky], having scattered over it a larger or smaller number of prominent, angular warty scales, which can be easily scraped off. The gills and stalk are white, and there is a large membranous collar, which hangs down from the upper part of the stem."

Clinical aspects

The clinical features of poisoning by *Amanita muscaria* are quite as characteristic as those in *Amanita phalloides* intoxication and should enable physicians to distinguish clearly between the two conditions. Unfortunately, poisonous fungi are usually gathered by the ignorant who sometimes eat a number of different varieties and consequently the symptoms in the patients point to the combined action of different toxic principles. In general, however, there is no difficulty in recognizing the character of the intoxication. In *Amanita muscaria* poisoning there is usually a very short interval between the ingestion of the fungi and the first signs of trouble. This prodromal stage varies from one or two to five or six hours depending upon the amount of the fungi eaten. Careful observation of this feature will frequently be of the greatest value in deciding upon the kind of intoxication which the cases present. In the severe cases the patients show an excessive salivation and perspiration, a flow of tears, nausea, retching, vomiting and diarrhoea with watery evacuations. The pulse may rarely be quickened, but it is usually slow and irregular. There is no fever. The respirations are accelerated and the patients dyspnoeic, the bronchi being filled with mucus. Mental symptoms are also present, particularly giddiness with confusion of ideas and rarely hallucinations. All these symptoms may vary in their intensity, at some times the gastro-intestinal predominating and at other times the mental. In light cases, where small quantities of the poisonous fungi are consumed, only an excessive salivation or perspiration may be noticed, with uneasiness and discomfort in the stomach and bowels, the symptoms subsiding spontaneously in a few hours. In the severe cases, the vomiting and diarrhoea may be so pronounced as to rid the alimentary canal of the offending material and the nervous symptoms then become the predominant ones. With large quantities of poison also the patients may show the nervous manifestations from the start, delirium, violent convulsions, and loss of consciousness developing in rapid succession and the patients sinking into a coma from which they can be roused with difficulty if at all. Rarely, consciousness is retained till the end, the patients dying from a paralysis of respiration. Finally, in many cases, after the preliminary attack of vomiting and diarrhoea, the patients sink into a deep sleep from which they wake several hours later profoundly prostrated but on the road to recovery. In such cases the effect of the poisoning passes off rapidly, the patients being restored to normal health within two or three days. There are no late effects or after-effects in *Amanita muscaria* intoxication, and the prognosis is always good if the patients recover from the preliminary symptoms. Chronic lesions such as develop in *Amanita phalloides* intoxication and are to be referred to the degenerative changes in the internal organs, do not occur with *Amanita muscaria*.[27] Rarely, the nervous manifestations of "muscaria" intoxication become much more pronounced than the alimentary and the patients become the victims of excitement and hallucinations evidencing many of the symptoms of alcoholic intoxication. This variety of poisoning is particularly common in Siberia where decoctions of *Amanita muscaria* are employed to induce orgies of drunkenness in which the most disgusting practices are followed, according to Kennan.[28] The physiological effect of the Siberian *Amanita muscaria* has never been clearly understood and the symptoms shown by the Koraks who employ the fungus as an intoxicant are seldom seen either in Europe or in America. Possibly the method of preserving the plants may alter the poisonous principles in them or possibly the Siberian plants do not contain the same poisonous substances as the European or American varieties. Death, however, is by no means an infrequent occurrence among the Koraks from an overdose of *Amanita muscaria* and, as we shall see later, the active principle of the European plants, muscarin, has also been obtained from the Siberian.

Autopsies upon individuals dead from the ingestion of *Amanita muscaria* have revealed surprisingly little. The pathological changes in the internal organs seen with *Amanita phalloides* are lacking, particularly the hepatic lesions. In general, the findings point to the action of a profound nerve poison (Ford[2]).

Poisonous constituents

As has already been indicated most of the early work upon the poisons in fungi was conducted upon poorly identified plants or upon lots of fungi containing a number of species, and it was not until the middle of the last century that any satisfactory work was accomplished upon *Amanita muscaria.* In 1869 Schmiedeberg and Koppe[29] took up the study of this fungus, investigating its poison from both the chemical and pharmacological standpoint. By the most careful work they showed that *Amanita muscaria* contains an active principle of definite chemical composition which they called muscarin. This was at first regarded as an alkaloid of the same general nature as strychnin and morphin but later work has shown that it is probably a complex ammonia derivative. Muscarin is an extremely active substance and is present in the fungus in but small amounts. Nevertheless, it is able to exert its characteristic effect, frequently with fatal outcome. Its principal action is upon the various organs of the body through the nervous system. It produces an increased secretion from the mucus membranes and from various glands, for instance, by its stimulation of the terminal filaments of the secretory nerves, and at the same time a paralysis of the heart and respiration by a corresponding stimulation of the inhibitory nerve endings of the vagus nerve. Atropin by its depressing action upon the same nerves which muscarin stimulates, is a perfect physiological antidote for the muscarin found in *Amanita muscaria* and also for synthetic muscarin which may be prepared by the oxidation of cholin. Its use, therefore, was at once suggested in *Amanita muscaria* poisoning.

The work of Schmiedeberg and Koppe upon *Amanita muscaria* was not accepted at once, nor did it fail to arouse considerable opposition. The cases of poisoning by this fungus presented such varied symptoms that it did not seem possible that they could all be referred to the one substance muscarin and this was particularly true in regard to the Siberian *Amanita muscaria.* It was soon shown by Schmiedeberg,[30] however, that the Russian fly amanitas had the same action upon animals as the European type and he was able to isolate muscarin from them. In addition to muscarin, however, Schmiedeberg[31] found later in this fungus evidences of another substance differing from muscarin in producing a dilatation of the pupils, thus acting like atropin. This second substance Schmiedeberg called muscaridin, and he believed that its presence in *Amanita muscaria* in greater or less amount would modify the action of the muscarin and thus the differences in intensity of the symptoms in *Amanita muscaria* poisoning would be explained. Muscaridin was later named "pilz-atropin" by Kobert[32] who states that it can be separated from commercial muscarin by its solubility in ether. It has, however, never been isolated from fresh *Amanita muscaria* plants. Finally, Kunkel[33] and other authorities maintain that the differences shown by the various cases of *Amanita muscaria* intoxication are due to the presence in the plant, in addition to muscarin, of a mixture of chemically related substances having entirely different pharmacological effects. This would account for the fact that atropin does not wholly neutralize the toxic action of *Amanita muscaria* upon animals despite the fact that it is a perfect physiological antidote for muscarin itself. This led Harmsen[34] to take up the question again and he has recently been able to show that extracts of *Amanita muscaria* are twice as toxic weight for weight as pure muscarin, and contain a poison which produces in animals long continued convulsions with a fatal outcome, this effect not being neutralized by atropin. This poison Harmsen calls the "pilztoxin." Its presence in *Amanita muscaria* has never been confirmed but some of the evidence, clinical and otherwise, indicates that muscarin may not be at all times the sole poison in *Amanita muscaria*.

It should be noted in this connection that the term muscarin is not the name of a specific chemical substance, but of a group of at least five substances with the same formula $C_5H_{15}NO_2$ and that the effects of these various compounds upon the animal organism are quite different from each other.* A complete discussion of the various muscarins, their properties and manner of preparation may be found in the works of Zellner[35] and Kobert.[32]

Treatment

The outlook in poisoning by *Amanita muscaria* is more hopeful that when *Amanita phalloides* has been ingested, because of the lack of chronic and degenerative lesions produced by the latter species. *Amanita muscaria* causes an acute intoxication which comes on soon after the ingestion of the fungus, develops rapidly, and is amenable to treatment. As we have indicated above, atropin is a perfect physiological antidote for muscarin. Whenever, therefore, the patients show evidence of muscarin poisoning such as lacrymation, salivation, contraction of the pupils, delirium, hallucinations, and coma, atropin should be administered at once and in large doses. At the same time the stomach and bowels should be emptied of the ingested material by the free use of emetics and purgatives. Even though the vomiting and diarrhoea are pronounced, drugs should be employed to increase this action since it is essential that all the fungi be removed and the absorption of poison be prevented. In refractory cases with bad heart action, respiratory distress and coma, atropin should be administered intravenously. In such cases atropin, indeed, offers the only hope of saving the patient's life. If the symptoms seen in cases of fungus intoxication do not point clearly to muscarin as the chief cause of the trouble but rather to other poisonous principles such as the pilz-atropin of Schmiedeberg and Kobert atropine naturally should not be administered. Finally, whenever the patients show symptoms referable to such poisons as Harmsen's "pilz-toxin" stimulants should be freely administered to tide the patients over periods of weakness and depression.

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* The bases cholin and neurin are closely related to muscarin and have both been reported in mushrooms. Neurin is very poisonous. According to Harnack (Arch. exp. Path. u. Pharmacol., 4, pp. 82 and 168 (1875)) the amanitin of Letellier and Speneux[17] is cholin. Clark and Kantor[49] found cholin in *Amanita muscaria* and other fungi. Hofmann (Dissertation, Zurich, 1906) discovered neurin in *A. muscaria*, but it is not certain whether it exists as such in the fungus or whether it is produced by processes of decomposition. The deadly prussic acid has been found in *Marasmius oreades* and *Clitocybe infundibuliformis* by Offner (Bull. Soc. Mycol. de France, 27, 242, 1912).

AMANITA PANTHERINA De Candolle

Amanita pantherina is a common amanita in Europe, particularly in France and Germany where it is regarded as a deadly poisonous species. Boehm[36] has isolated muscarin from this plant in Germany so that the active principle is probably the same as that of the "muscaria." The species is very common in Japan and Inoko[7] believes that it represents *Amanita muscaria* there. Poisoning is quite frequent in that country from its accidental consumption but the symptoms are by no means the same as with the true "muscaria." Delirium and hallucinations with visions of beautiful vari-colored objects predominate over the gastro-intestinal symptoms, the effects being a little like those described for the Siberian "muscaria." The "pantherina" is also said to be used in Japan to produce mushroom drunkenness. Inoko has isolated muscarin from the Japanese *Amanita pantherina* and has also found in it a substance like the "pilz-atropin" of *Amanita muscaria*. *Amanita pantherina* is not common in America but Atkinson[37] believes that his species *Amanita cothurnata* may represent a light colored form of "pantherina" here. In the only report upon *Amanita pantherina* thus far published in America (Ford and Sherrick[38]) no evidence was presented to show that our species contains muscarin. For the present both the real "pantherina" and Atkinson's "cothurnata" should be avoided by collectors. Should symptoms of muscarin intoxication follow their ingestion, the treatment should be along the lines already indicated, namely, complete evacuation of stomach and bowels and large doses of atropin.

EDIBLE AMANITAS

Certain varieties of amanitas have long been known to be edible and indeed have been highly prized by epicures. The most important species of this character are *Amanita caesarea* (Caesar's agaric), *Amanita rubescens* Persoon and *Amanita junquillea* Quelet. No report has appeared in the literature in regard to the chemical properties of *Amanita caesarea* but Ford[39] has shown that *Amanita rubescens* has no toxic action upon animals. *Amanita junquillea* likewise is free from poisonous properties (Ford and Brush[40]). Such species, while possibly safe in the hands of experts should not be collected by amateurs owing to the difficulty in properly identifying them. There are also a number of amanitas which have no poisonous action upon animals, the properties of which have not been clearly established by experience. Among such species are *Amanita frostiana* Peck (Ford[25]) and *Amanita solitaria* Bulliard (Ford[39]). Owing to the resemblance of *Amanita frostiana* to *Amanita muscaria* and to the difficulties in the recognition of *Amanita solitaria* it would be unwise to recommend either of these species. Much the same may be said of *Agaricus amygdalinus* Curtis possibly identical with *Agaricus fabaceus* Berkeley which causes unpleasant symptoms on ingestion but which has never been reported as causing serious illness (Ford and Sherrick[38]).

LEPIOTA MORGANI Peck

The "green-spored" lepiota is a handsome plant growing with great freedom in the Ohio valley. In its favorite localities *Lepiota morgani* thrives in grassy pastures as well as in woods and this fact has been the cause of confusing it with the edible *Agaricus campestris*. The green spores of this fungus ought to serve as a sufficiently striking characteristic to prevent mistaking it for any edible fungus. Chestnut[41] has collected evidence that showed that *Lepiota morgani* often has caused serious illness and at least one death. His physiological experiments indicated that specimens of this plant from the District of Columbia were definitely poisonous to animals and that heating destroyed the greater part of its toxic properties.

CLITOCYBE ILLUDENS Schweinitz

There has always been a tradition that this species is poisonous and not pleasant to eat. Several cases of poisoning from its consumption are recorded but it seems not to have caused fatal results. *Clitocybe illudens* grows in clumps at the base of tree trunks where its bright orange-brown color and phosphorescent glow at night seem to have attracted unfavorable attention. Ford[42] has reported that this fungus produces an acute intoxication in guinea pigs and that boiling the extracts of the plant seems to destroy the toxic properties as is sometimes the case with *Amanita muscaria.* Recently Clark and Smith[11] have investigated *Clitocybe illudens* and have found that upon the exposed frog heart it exerts a typical muscarin effect, which is neutralized at once by the application of atropin solutions. On the whole we may safely say that *Clitocybe illudens* is a dangerous fungus since it contains a muscarin-like substance having a powerful action on the nervous system.

CLITOCYBE DEALBATA SUDORIFICA Peck

The original species, *Clitocybe dealbata* Sowerby, has usually been considered harmless but Peck[43] investigated a reported case of poisoning by it and has found that a form of *Clitocybe dealbata* causes profuse perspiration and discomfort. In consequence, Peck gave this form the varietal name *sudorifica* and advised caution in its use as food. Ford and Sherrick[44] have found that this fungus causes effects upon animals that are nearly identical with those produced by *Amanita muscaria.* As mentioned in the discussion of *Clitocybe illudens,* Clark and Smith have found that *Clitocybe illudens* shows a typical muscarin action also; therefore it seems likely that these two clitocybes may contain nerve poisons nearly as active as muscarin.

LACTARIUS TORMINOSUS Fries

As a general rule, specimens of the genus *Lactarius* are edible but this particular species has always been looked upon askance by mushroom eaters because of the painful gastro-intestinal disorders it causes. Ford[42] has studied its action on animals and has demonstrated that it can produce an acute intoxication with only a few of the characteristic muscarin symptoms. It is worthy of note that the poison is destroyed by heating, as previously reported by Kunkel.[45] Goldman[46] has reported cases of poisoning by *Lactarius torminosus* in Germany.

RUSSULA EMETICA Fries

The tendency of this brilliant species to cause gastro-intestinal disturbances with vomiting is well known and this reputation has prevented its use as food. Kobert[32] has isolated three basic substances from it; cholin, muscarin, and an atropin-like substance already mentioned in the discussion of *Amanita muscaria.* The emetic properties of this fungus are usually sufficient to cause its expulsion as soon as the material reaches the stomach and thus prevent absorption of the poison.

PHOLIOTA AUTUMNALIS Peck

Peck[47] has called attention to the fact that this supposedly harmless mushroom may be the cause of fatal poisoning and Ford and Sherrick[38] have studied its action on animals and have shown that it is acutely toxic to them. At the autopsy the hearts were found greatly dilated in every case and atropin did not neutralize this peculiar heart-dilating effect. Evidently the poison is a powerful one of unknown nature.

INOCYBE INFIDA (Peck) Earle

This is so small a plant that it is not likely to fall into the hands of mushroom eaters. Murrill,[48] however, has recorded the poisoning of a family of several persons who had eaten *Inocybe infida* by mistake for another similar but edible fungus. Clark and Kantor[49] have isolated from this plant, by methods planned to extract muscarin from *Amanita muscaria,* a small amount of a poison causing long continued paralysis in frogs. The symptoms shown by the frogs were not typical of muscarin but did indicate a definite and powerful action on the nervous system. In a later series of experiments Clark and Smith[11] applied the same extraction methods to both *Inocybe infida* and *Clitocybe illudens,* obtaining substances which had a characteristic muscarin effect upon the frog's heart, the effect being neutralized by atropin. Further investigations are needed upon these fungi to determine more clearly the relationship of their toxic principles to those found in *Amanita muscaria.*

INOCYBE INFELIX Peck

While this plant has never been investigated from the standpoint of edibility, it has been shown by Ford[42] that it contains a definite poison for both rabbits and guinea pigs, which resists desiccation and boiling. In these animals the fungous extract in small doses produced a deep sleep from which they awoke in a few hours apparently well, while with large doses profound and acute intoxication developed from which they died in a short time. The animals did not show the characteristic "muscaria" effects and Ford was therefore led to conclude that *Inocybe infelix* contained a narcotic poison of some sort. Further work is required in regard to the qualities of this species, particularly since the symptoms noted in the poisoned animals are not entirely inconsistent with muscarin poisoning.

INOCYBE DECIPIENS Bresadola

This fungus has not thus far been tested for edibility, but it has been shown by Ford and Sherrick[38] that it contains a poison belonging to the muscarin-pilocarpin series. In large animals it causes an acute intoxication resembling that produced by *Amanita muscaria* with lacrymation, salivation, contracted pupils, and labored respiration as the chief symptoms. Upon the frog's heart the fungus extracts had the typical "muscaria" effect causing a stoppage in diastole which was neutralized by atropin. *Inocybe decipiens* should, therefore, be grouped with the deadly poisonous fungi, as liable to contain muscarin.

THE HEBELOMAS

Kobert[50] states that both *Hebeloma rimosum* and *Hebeloma fastibile* contain muscarin-like poisons, the nature of which is unknown. Mycologists have usually regarded the genus Hebeloma as unfit for food. At the present time little is known of American specimens of this group, either from the systematic or toxicological standpoint.

THE ENTOLOMAS

In Europe, both *Entoloma lividum* and *Entoloma sinuatum* are classed among the poisonous fungi. According to a recent collection of cases by Sartory[12] in France, *Entoloma lividum* is an extremely dangerous fungus, causing severe illness and occasionally death. Sartory believes that *Entoloma lividum* is nearly as poisonous as some of the various forms of *Amanita phalloides.*

THE PANAEOLUS SPECIES

In this group, *Panaeolus papillionaceus* and *Panaeolus retirugis* are reputed to produce hilarity and a mild intoxication in man. Ford[42] has studied an American form of *Panaeolus retirugis* and has found it to be poisonous to guinea pigs, producing in them a peculiar kind of intoxication which resulted in death but left no lesions apparent at autopsy.

BOLETUS LURIDUS Schaeffer

Among the usually harmless Polyporaceae this species has always had an unsavory reputation. Boehm[36] has isolated muscarin from *Boletus luridus* and has thus shown that there is good ground for including this boletus among the poisonous fungi. *Boletus luridus* is not a common plant in America and may not exist here at all in the form found in Europe.

BOLETUS SATANUS Lenz

Besides the *Boletus luridus* just mentioned it is likely that *Boletus satanas* also contains a poisonous principle· Utz[51] found a basic substance in this fungus and named it boletin but from its chemical properties and its physiological action we may conclude that he probably was dealing with muscarin. Like *Boletus luridus* it is uncertain whether this species occurs in America. It is often said that one is never in danger from eating any boletus but the possibility of muscarin occurring in some of this group is enough to cause one to use caution in eating unfamiliar species, even if nothing worse than gastro-intestinal disturbances are produced.

BOLETUS MINIATO-OLIVACEUS Frost

In 1899 Collins[52] reported cases of poisoning from eating *Boletus miniato-olivaceus* variety *sensibilis* but nothing more was learned of this species until recently when Ford and Sherrick[44] made experiments with it. They showed that extracts from the plant killed guinea pigs in several days but that rabbits were not affected. The guinea pigs became emaciated but nothing characteristic was noted at autopsy.

POLYPORUS OFFICINALIS Fries

From this polypore a definite poisonous substance has been isolated, having the name agaricinic acid, and the chemical formula $C_{14}H_{27}OH(COOH)_2$. This substance is used to a small extent in medicine to lessen excessive perspiration but cannot be given in large doses as it causes vomiting and purging by its strong irritating effect upon the mucous membranes. Jahns[53] and also Hofmeister[54] have made careful studies on the preparation and the physiological action of agaricinic acid.

GYROMYTRA ESCULENTA FRIES

Years ago the poisoning from the false morel was reported frequently in Germany but within the past few years the only note of such accidents is that of Lövegren[55] who has described several cases in which the lesions pointed to a hemolytic intoxication. The action of this fungus upon man and upon animals is by no means definite, however, and much work must be done before the matter is clarified. The European variety of the false morel, *Morchella esculenta* or *Gyromytra esculenta,* has been shown by the researches of Boehm and Külz[56] to contain a hemolytic poison, helvellic acid, and this agrees with the observations which have been made clinically. Accidents from poisonous morels have not been reported in America and no observations have thus far been made with this fungus collected in America except on one occasion (Ford and Sherrick[38]) when it was found to have no hemolytic action or poisonous effect upon animals.

PROPHYLAXIS

Mushrooms are usually eaten for their flavor which makes them an agreeable relish and food-accessory rather than a staple article of diet. There is no general cook-book test to distinguish the dangerous fungi from the edible ones. The habits and appearance of the poisonous species must be studied until one may recognize them with the same ease and certainty as any of the common plants of our gardens. Neglect of this precaution in gathering mushrooms for the table will sooner or later cause a typical attack of poisoning, and in such cases it should be remembered that the mortality is often as high as in any of the most fatal diseases. The rapidly increasing number of deaths in this country from mushroom poisoning shows that some effort must be made to disseminate exact information about the dangerous species in order to prevent unnecessary suffering and death.

There is a tradition in this country and Europe that treating *Amanita muscaria* (Coville[57]) with vinegar and salt water removes the poisonous constituents. This treatment if repeated several times would probably remove muscarin and similar substances but the danger from incomplete extraction of the poison is still too great to recommend its use. In the case of *Amanita phalloides,* Radais and Sartory[58] have shown that such treatments do not reduce the toxicity of the fungus in spite of popular belief to the contrary. There is little doubt that in some countries people habitually eat *Amanita muscaria* in small quantities, both treated and untreated, with no apparent signs of poisoning, but this does not warrant us in ever allowing ourselves to experiment upon the edibility of such poisonous fungi. Generally, in this country, no one eats *Amanita muscaria* because of its well known dangers. In some of our investigations (Clark and Smith[11]) on American specimens of this plant from different localities we found apparently great differences in toxicity, possibly due to local variation. Furthermore, under certain conditions, heat may destroy the poisons in *Amanita muscaria* as reported by Ford[42] and others, but neither does this observation warrant us in concluding that the dangers from eating this fungus are overestimated.

The first necessary prophylactic measure is to impress upon mushroom lovers that *there is no easy empirical test to distinguish between the edible and poisonous fungi.* No one should eat an unfamiliar mushroom until it has been identified as a harmless species by a well-trained mycologist. It is not difficult to learn to know fungi at a glance if one is willing to study them closely and to remember the points of difference in form, color, and habit among the various species. Unfortunately, there are a few "mushroom handbooks" in this country, which are unfailing sources of misinformation, and they have evidently been written by people of no training and poor judgment. In one case, color plates of *Amanita muscaria* and *Amanita caesaria* have the names of these two species transposed. Identifications based on pictures are dangerous unless the publication of such unreliable books is prevented. After all, the number of poisonous species is very small and when they are eliminated there are still many desirable fungi which are perfectly safe esculents.

So far we have mentioned only the prophylactic measures to be taken in eating wild mushrooms gathered in the fields, but there is a broader phase to be considered; this is the question of mushrooms in the public markets. If these markets are supplied by wild fungi gathered for the purpose it is necessary to see that no poisonous species become mixed with the others. In European countries many of the public markets have an official mushroom inspector, whose duty it is to examine all lots of fungi before they are exposed for sale and to condemn all fungi not known to be entirely harmless to man. With the increasing taste for mushrooms in this country and the larger stocks carried during the season, it may become necessary for us to control our mushroom supply in a similar manner. Several deaths have been caused by poisonous fungi bought in our public markets.

Even the use of cultivated mushrooms does not guarantee immunity from trouble by poisoning since it is believed by several investigators that harmless fungi may become poisonous if kept too long before consumption (Kobert[59]). This often happens in markets and restaurants where mushrooms become slightly decomposed before they can be sold. Another danger is that cooked mushrooms may develop toxic properties after being kept during the summer weather and again served at subsequent meals (Frey[60]). On chemical ground it is easy to see that the unstable nitrogenous substances in edible fungi could easily be changed into toxic constituents by the action of microörganisms. This is another matter that ought to be studied by chemical and pharmacological methods before we can feel at all satisfied with our present knowledge of the properties of poisonous mushrooms.

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